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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Display Date 8/2/05
Publication Date 8/3/05
Certifier J. Cook

Food and Drug Administration

[Docket No. 2004N–0355]

Critical Path Initiative; Developing Prevention Therapies; Planning of Workshop

AGENCY: Food and Drug Administration, HHS.

ACTION: Request for Comments.

SUMMARY: The Food and Drug Administration (FDA) is planning a 2-day workshop to explore approaches and potential obstacles to developing drugs, disease biomarkers, medical devices, and vaccines to prevent or reduce the risk of illness. The agency plans to hold the workshop as part of its Critical Path Initiative. Speakers at the workshop will be asked to discuss the challenges in developing chemoprevention therapies (i.e., prevention therapies other than lifestyle changes, dietary supplements, or dietary choices that could reduce the risk of certain illnesses such as cancer, diabetes, and obesity). Because prevention of illness is widely recognized to be an important goal and the possible scope of this workshop is very broad, FDA welcomes comments related to the scope of this workshop.

DATES: Submit written or electronic comments by [*insert date 90 days after date of publication in the* **Federal Register**]. General comments are welcome at any time.

ADDRESSES: The FDA invites you to submit written comments on the proposed scope of the workshop. Please submit comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane,

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rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments.*

FOR FURTHER INFORMATION CONTACT: Nancy Stanisic, Center for Drug Evaluation and Research (HFD–05), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852, 301–827–1660, FAX: 301–443–9718, e-mail: *Stanisicn@cder.fda.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

The development of methods to prevent disease has been the single, most effective advance in healthcare in the past century, particularly in developed countries. The widespread ravages of smallpox, infantile diarrhea, plague, cholera, typhoid, and polio are gone from the United States.

The challenge that lies ahead is to prevent the diseases that still ravage our population, including: Heart disease, cancer, diabetes, Alzheimer's disease, and others. In recent decades, substantial effort has been made in the chemoprevention or early intervention for some of the top killers in the United States, notably cardiovascular disease and some cancers. Examples of effective preventive interventions include the aggressive treatment of hypertension to reduce the risk of stroke, statins to lower cholesterol and decrease the risk of a myocardial infarction, the use of low-dose aspirin and beta blockers to prevent death in patients after a myocardial infarction, tamoxifen to reduce the risk of recurrent breast cancer, aggressive control of blood glucose to reduce the long-term consequences of diabetes, and flu and pneumonia vaccination programs to reduce morbidity and mortality.

Significant advances have also been made in the early identification of healthy individuals at risk of developing disease. Examples of predictors

include genetic markers, such as BRCA 1 and 2 for malignancy; pap tests for identification of patients at risk for cervical cancer; genetic alpha–1–antitrypsin deficiency for lung disease; colonoscopy to identify polyps that predict an increased risk of colon cancer; and family history, obesity, and ethnicity for type II diabetes mellitus. Ongoing work in genomics and proteomics promises to identify additional markers to predict specific health risks and potential targets for intervention.

Although markers have been identified, candidate therapies require prospective testing in clinical trials. The design and conduct of chemoprevention trials offer substantial challenges. For example, in the Women's Health Initiative, we learned that the epidemiologic study results of the use of conjugated estrogens to prevent heart disease could not be replicated in the randomized, double-blind clinical trial setting. The Celebrex trial gives another example that prevention studies, in this case polyp prevention trials, must be of sufficient duration to ensure that the risks of long-term use of drugs are captured. These risks may be unexpected and the Data Safety Monitoring Boards need to pay careful attention as signals arise.

II. FDA Critical Path

On March 16, 2004, FDA published its Critical Path report,[1] aimed at identifying potential problems and solutions to ensure that breakthroughs in medical science can be efficiently translated to safe, effective, and available medical products. In the report, FDA underscored the importance of FDA collaboration with academic researchers, product developers, patient groups, and other stakeholders to make the critical path more predictable and less

[1] For the complete report, see *http://www.fda.gov/oc/initiatives/criticalpath.*

costly. This workshop and any activities that result from the workshop are part of that broad effort.

III. Topics Related to Planning the Public Workshop

Because the range of potential topics that could be discussed at such a workshop is so wide, we are seeking the public's input on what key topics should be addressed at this initial meeting.

Although the prefix "chemo-" is often used in relation to treatments for cancer, we are using the term "chemoprevention" in this notice to describe prevention therapies other than lifestyle changes, dietary supplements, or dietary choices that could reduce the risk of certain illnesses. We welcome comments on the use of the term "chemoprevention."

What follows is a list of topics and questions we have identified for possible discussion at the workshop. We welcome comment on whether these topics and questions are appropriate for discussion at a workshop on chemoprevention therapies? Are there other related issues that should be discussed at the workshop? What are they? Currently, we envision a 2-day workshop, with the first day devoted to identifying hurdles and challenges in designing and implementing chemoprevention studies from a broad perspective. The second day may consist of breakout sessions devoted to specific diseases or disease categories. We welcome input on the format for the 2-day workshop.

Does the following list of questions reflect the kinds of questions we should try to answer at a 2-day workshop on chemoprevention therapies? What questions would you be interested in having answered? In addition to the following topics, what other topics should be included in the scope of the meeting?

1. What have our successes been so far, and what lessons have we learned from past experience with regard to the development of the following preventive therapies:

a. Vaccines

b. Cardiovascular disease

c. Cancer

i Breast

ii Colon polyps

2. Which diseases are the most promising with regard to development of chemoprevention therapies?

3. What options are available now for identifying populations at risk for those diseases?

a. Screening

b. Genomics

c. Other

4. What techniques are available for assessing the risks and benefits of new therapies in prevention?

5. How much risk from the candidate therapy is acceptable?

6. Are there specific regulatory concerns in developing chemopreventions (e.g., Long trials, safety and efficacy issues, registries)? And what steps can FDA take to facilitate development in this area, such as the following?

a. Mechanisms to streamline the regulatory process

b. Mechanisms to facilitate the scientific process and clinical trials

i. To better and more efficiently answer questions regarding product efficacy

ii. To better and more efficiently answer questions regarding product safety

7. What are some of the obstacles facing manufacturers who wish to develop new or existing compounds for chemoprevention? For example, are there specific industry perspectives that need to be considered?

8. What patient perspectives are important to consider?

We have proposed the following topics and questions for discussion on the second day during breakout sessions. Are these appropriate? What other issues would you be interested in discussing at these breakout sessions?

1. Cancer prevention issues

a. What characteristics of particular cancers make prevention promising?

b. What characteristics from epidemiologic, early trials, or other models make particular drugs promising?

c. What trial design issues should be addressed (e.g., endpoints, surrogates, population, adverse event data collection)?

d. Are there obstacles to marketing prevention drugs?

2. Cardiovascular prevention issues

a. What characteristics of cardiovascular disease make prevention promising?

b. What characteristics from epidemiologic, early trials, or other models make particular drugs promising?

c. What trial design issues should be addressed (e.g., endpoints, surrogates, population, adverse event data collection)?

d. Are there obstacles to marketing prevention drugs?

3. Cerebrovascular prevention issues

a. What characteristics of cerebrovascular disease make prevention promising?

b. What characteristics from epidemiologic, early trials, or other models make particular drugs promising?

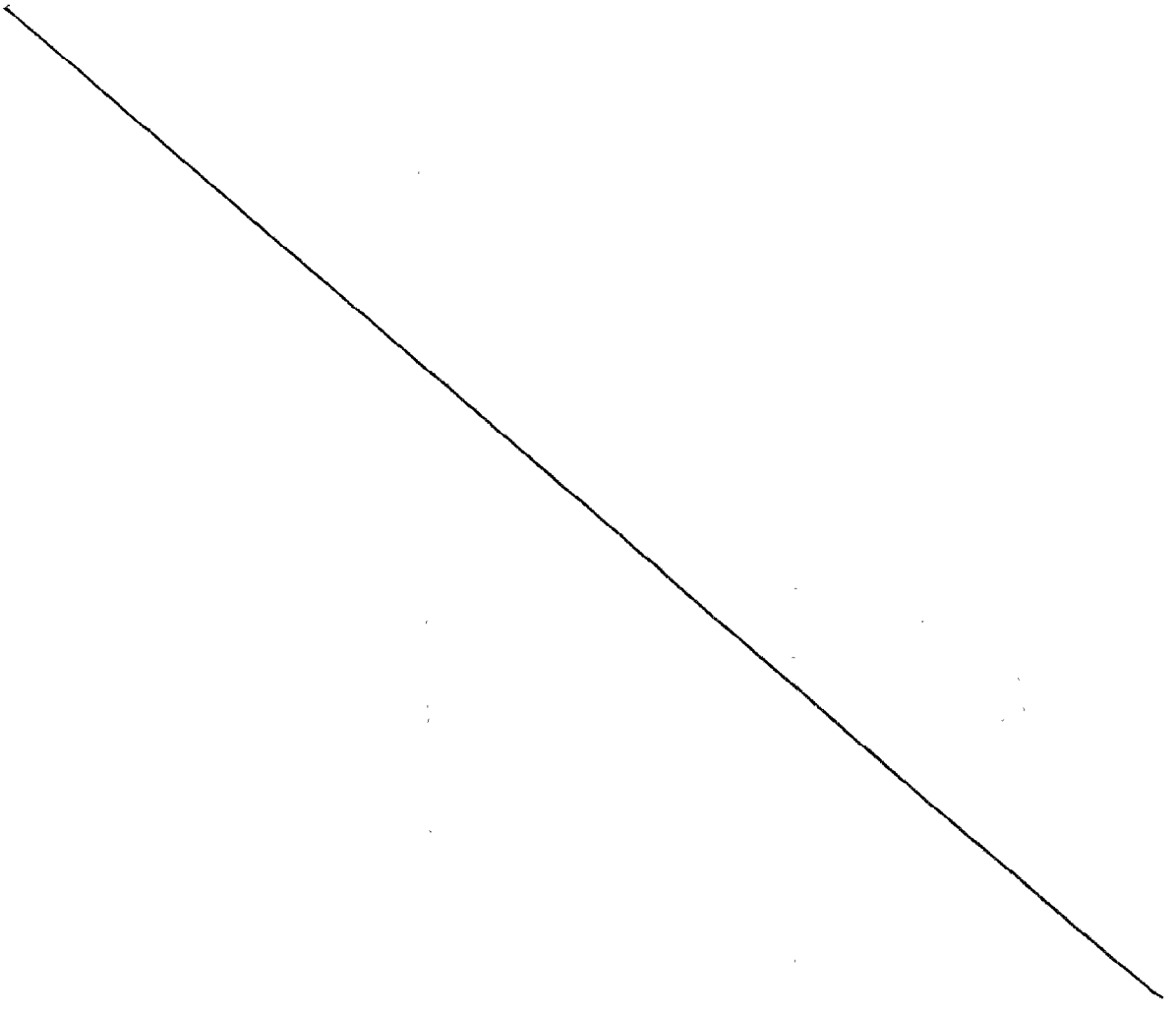
c. What trial design issues should be addressed (e.g., endpoints, surrogates, population, adverse event data collection)?

d. Are there obstacles to marketing prevention drugs?

4. What other conditions should be discussed?

IV. Submission of Comments

Interested persons may submit written or electronic comments to the Division of Dockets Management (see **ADDRESSES**). Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received



comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday. You can also view received comments on the Internet at *http://www.fda.gov/ohrms/dockets/dockets/dockets.htm*

Dated: 7/28/05
July 28, 2005.

Jeffrey Shuren,
Assistant Commissioner for Policy.

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[FR Doc. 05–????? Filed ??–??–05; 8:45 am]

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